Amendments to the Claims/Listing of Claims

Please amend claims 15, 120, 124, 129 and 134, and add claim 142 as follows. In addition, please cancel claim 19 without prejudice. This listing of claims will replace all prior versions, and listings, of claims in the application.

1-14 (Canceled)

15. (Currently amended) A method for developing improved ligands binding to PIM kinase, **said method** comprising **in order:**

conducting enzymatic assays with one or more PIM kinases and molecular scaffold compounds, thereby identifying a molecular scaffold compound that binds **with low, very low or extremely low affinity** to a binding site of **[[the]] said** PIM kinase**s**;

~~preparing~~ **synthesizing** a derivative of the **above-identified** molecular scaffold compound; and

testing said derivative **by enzymatic assay** for binding to PIM with increased specificity relative to the **above-identified** molecular scaffold compound, wherein said binding to PIM with increased specificity is indicative that said derivative is an improved ligand.

16. (Previously presented) The method of claim 15, wherein said molecular scaffold compound binds to at least 5 different human kinases.

17. (Previously presented) The method of claim 15, wherein said molecular scaffold compound binds to at least 10 different human kinases.

18. (Original) The method of claim 15, wherein said PIM is PIM-1, PIM-2, PIM-3, or any combination of at least two of PIM-1, PIM-2, and PIM-3.

19-119 (Canceled)

120. (Currently amended) An in vitro method for obtaining improved ligands binding to PIM-1, **said method** comprising

conducting enzymatic assays employing PIM-1 and candidate molecular scaffold compounds, thereby identifying a molecular scaffold compound that binds to PIM-1 **with low, very low or extremely low affinity** and interacts with one or more PIM-1 residues selected from the group consisting of residue 49, 52, 65, 67, 121, 128, and 186;

~~**preparing**~~ **synthesizing** a derivative of the molecular scaffold compound; and

conducting enzymatic assays with PIM-1 and said derivative, thereby determining whether **[[the]] said** derivative binds to PIM-1 with greater affinity or greater specificity or both than said molecular scaffold compound, wherein binding with greater affinity or greater specificity or both indicates that said derivative is an improved ligand.

121. (Previously presented) The method of claim 120, wherein said derivative has at least 10-fold greater affinity or specificity or both than said molecular scaffold compound.

122. (Previously presented) The method of claim 120, wherein said derivative has at least 100-fold greater affinity or specificity or both than said molecular scaffold compound.

123. (Previously presented) The method of claim 120, wherein said molecular scaffold compound has a chemical structure of Formula I, Formula II, or Formula III.

124. (Currently amended) An in vitro method for developing ligands specific for PIM-1, **said method** comprising

conducting enzymatic assays with a plurality of different kinases and candidate molecular scaffold compounds, thereby identifying a molecular scaffold compound that binds to a plurality of different kinases **with low, very low or extremely low affinity**;

~~**preparing**~~ **synthesizing** a derivative of **[[the]] said** molecular scaffold compound; and

testing said derivative by enzymatic assay for activity on PIM-1, thereby determining whether the derivative has greater specificity for PIM-1 than said molecular scaffold compound.

125. (Previously presented) The method of claim 124, wherein said molecular scaffold compound binds to PIM-1 with an affinity at least 10-fold greater than for binding to any of said plurality of different kinases.

126. (Previously presented) The method of claim 124, wherein said molecular scaffold compound interacts with at least one PIM-1 residue selected from the group consisting of residue 49, 52, 65, 67, 121, 128, and 186.

127. (Previously presented) The method of claim 124, wherein said molecular scaffold compound is a compound of Formula I, Formular II, or Formula III.

128. (Previously presented) The method of claim 124, wherein said molecular scaffold compound binds weakly to said plurality of kinases.

129. (Currently amended) An in vitro method for developing ligands binding to PIM-1, **said method** comprising

conducting enzymatic assays with PIM-1 and molecular scaffold compounds, thereby identifying as molecular scaffolds one or more compounds that bind to a binding site of PIM-1 **with low, very low, or extremely low affinity**;

determining the orientation of at least one **of the above-identified** molecular scaffold**s** in co-crystals with PIM-1;

based on said determining step, identifying chemical structures of said molecular scaffolds, that, when modified, alter the binding affinity or binding specificity or both between the molecular scaffold and PIM-1; and

synthesizing a ligand wherein one or more of the **above-identified** chemical structures of the molecular scaffold is modified to provide a ligand that binds to PIM-1 with altered binding affinity or binding specificity or both.

130. (Previously presented) The method of claim 129, wherein said molecular scaffold is a weak binding compound.

131. (Previously presented) The method of claim 129, wherein said molecular scaffold binds to a plurality of kinases.

132. (Previously presented) The method of claim 129, wherein said molecular scaffold interacts with one or more PIM-1 residues selected from the group consisting of residues 49, 52, 65, 67, 121, 128, and 186.

133. (Previously presented) The method of claim 129, wherein said molecular scaffold has a chemical structure of Formula 1, Formula II, or Formula III.

134. (Currently amended) An in vitro method for developing a ligand for a kinase comprising conserved residues matching one or more PIM-1 residues selected from the group consisting of residues 49, 52, 65, 67, 121, 128, and 186, **said method** comprising

conducting enzymatic assays with PIM-1 and a compound of Formula I, Formula II or Formula III, thereby determining whether **[[a]] the** compound of Formula I, Formula II, or Formula III binds to said kinase **with low, very low or extremely low affinity**;

identifying chemical structures of said compound, that, when modified, alter the binding affinity or binding specificity or both between the compound and said kinase; and

based on said identifying step, synthesizing a ligand wherein one or more of the chemical structures of the compound is modified to provide a ligand that binds to said kinase with altered binding affinity or binding specificity or both compared to said compound.

135. (Previously presented) The method of claim 134, wherein said kinase comprises conserved residues matching at least 2 PIM-1 residues selected from the group consisting of residues 49, 52, 65, 67, 121, 128, and 186.

136. (Previously presented) The method of claim 134, wherein said kinase comprises conserved residues matching PIM-1 residues 49, 52, 65, 67, 121, 128, and 186.

137. (Previously presented) The method of claim 134, further comprising determining whether said compound modulates said kinase.

138. (Previously presented) The method of claim 134, wherein said determining comprises computer fitting said compound in a binding site of said kinase.

139. (Previously presented) The method of claim 134, further comprising forming a co-crystal of said kinase and said compound.

140. (Previously presented) The method of claim 139, further comprising determining the binding orientation of said compound with said kinase.

141. (Previously presented) The method of claim 134, wherein said kinase has at least 25% sequence identity to full-length PIM-1.

142. (New) The method according to Claim 15, wherein

said PIM is PIM-1; and

said derivative comprises a core structure selected from the group consisting of Formula I, Formula II, and Formula III.